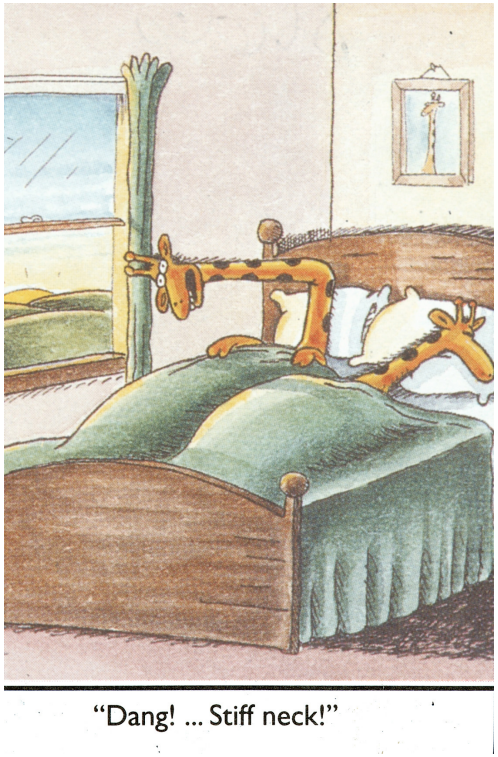
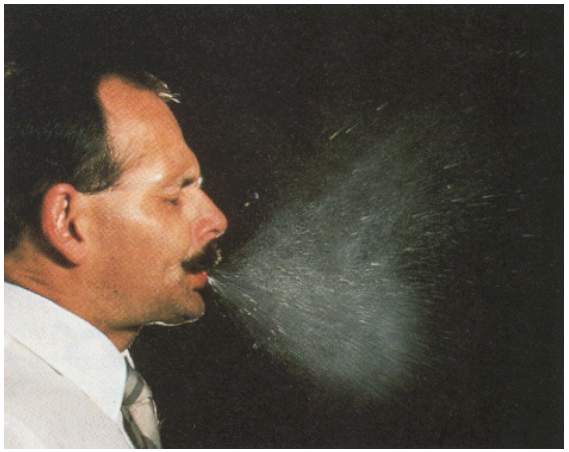
# Viral Infections – any Questions?

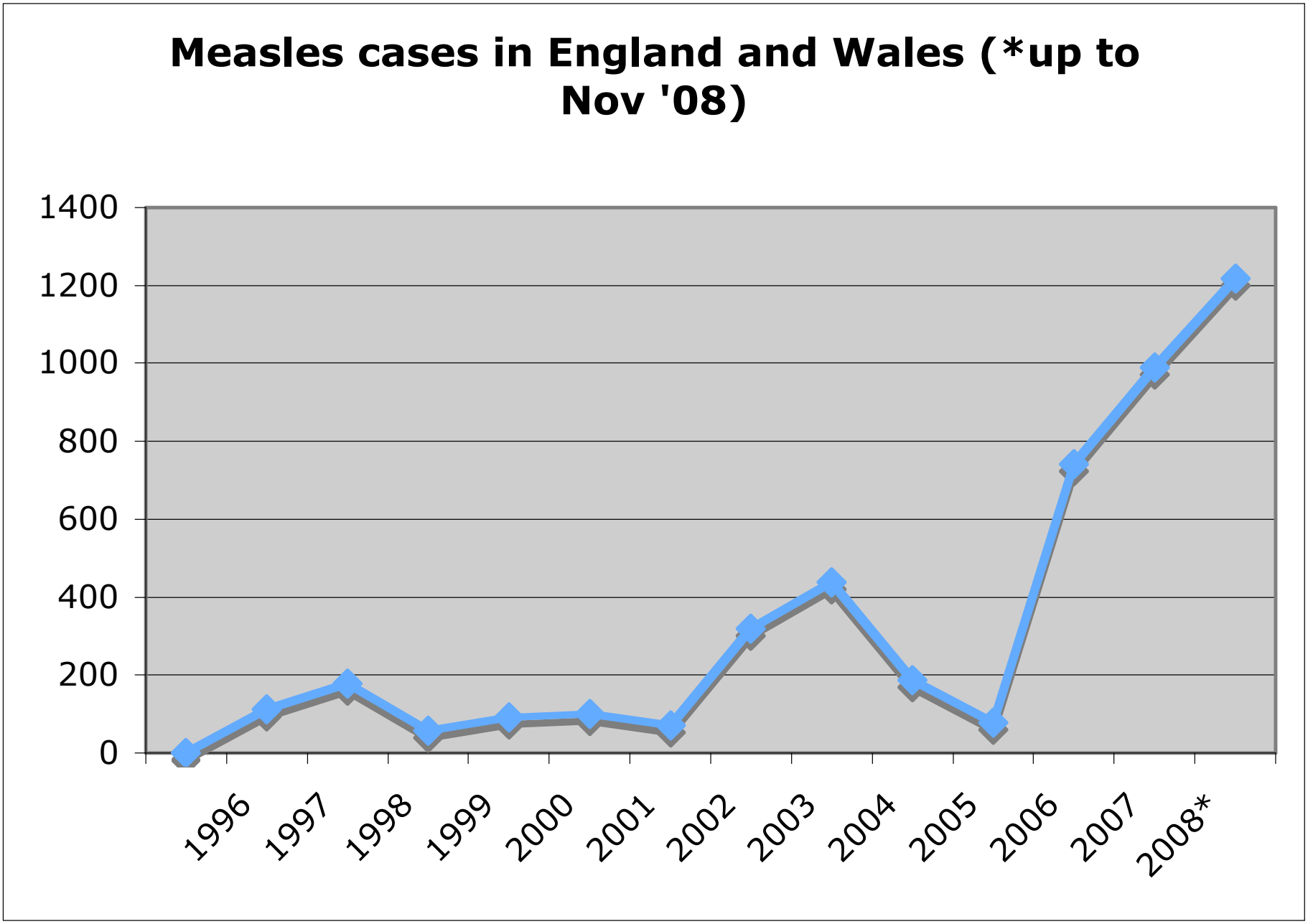



Katie Jeffery
Consultant Virologist

# Common phone calls to Virology

- Pregnancy – exposure to rash illness
- Chicken pox in pregnancy
- Immunosuppression – chicken pox exposure
- Hepatitis B immunisation
- Needlestick injury in the Community


Measles cases in England and Wales (*up to Nov '08)
1400
1200
1000
800
600
400
200
0
1996
1997
1998
1999
2000
2001
2002
2003
2004
2005
2006
2007
2008*

# ‘Spot’ diagnosis

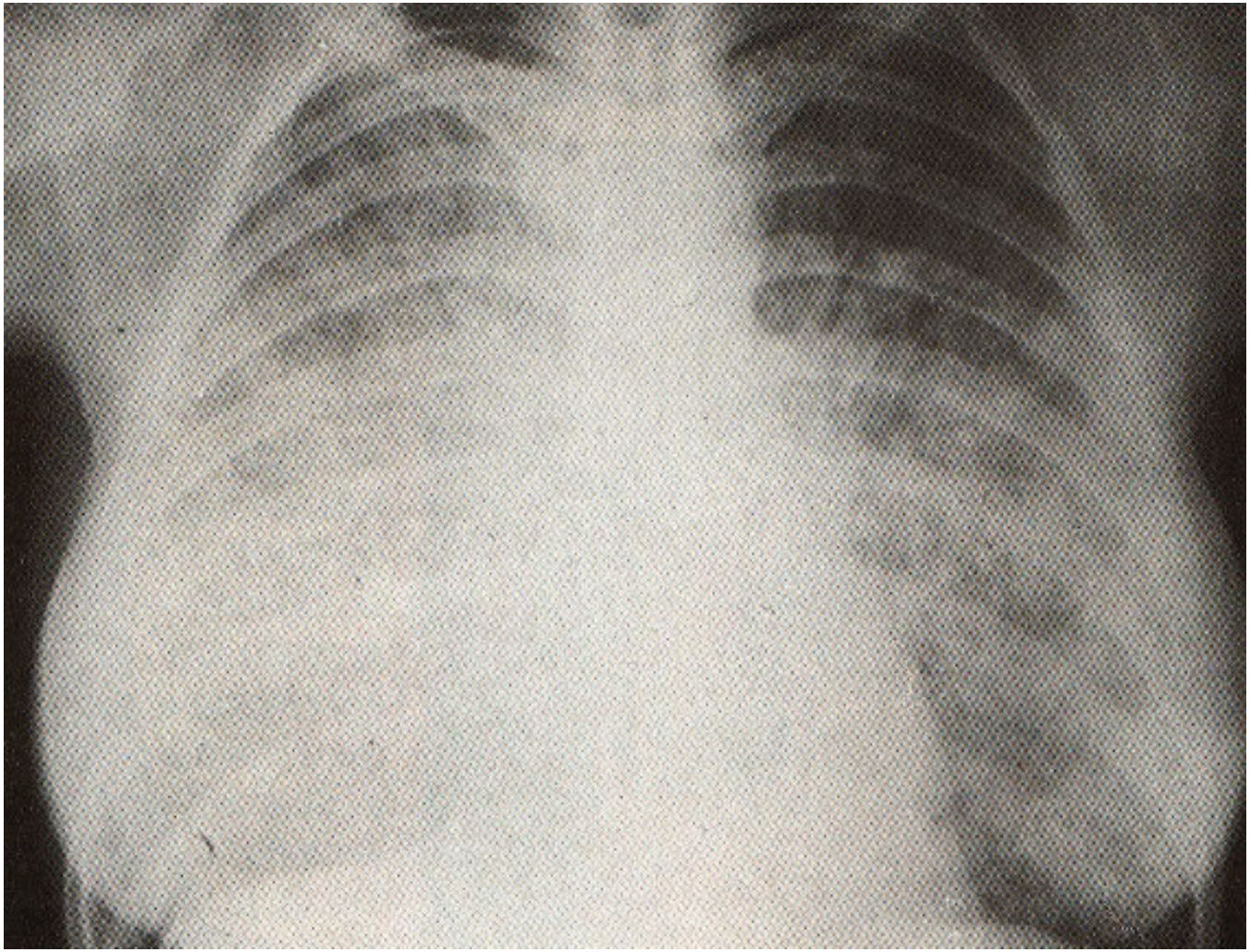
- 27 year old nursery nurse
- 2 day history of fever and malaise
- 1 day sore mouth and itchy ‘spots’ on her trunk

- What is the diagnosis and how might it be confirmed?
- What are the important complications?
- What are the risks of infection in pregnancy?
- What are the infection control implications?

# Complications of primary VZV infection:

- Adults
  - varicella pneumonia
  - bacterial pneumonia
- Children
  - encephalitis / ataxia
  - Secondary bacterial infections (Group A Streptococcus, Staphylococcus aureus)

Varicella pneumonitis



Congenital Varicella syndrome

# Prevention of Primary VZV infection

- **Isolation** of patients with varicella or zoster from vulnerable contacts
- **Post-exposure prophylaxis** with varicella-zoster immunoglobulin (VZIG) indicated for individuals
  1) at increased risk of severe varicella **and**
  2) seronegative for VZV **and**
  3) significant exposure to chicken pox or zoster
- **Active vaccination** of susceptible individuals or their contacts

# Varicella vaccination

- First licensed herpes vaccine

# Why do we want a vaccine for a ‘benign’ childhood illness?

25 chicken pox deaths in UK adults each year

Adults account for 80% of the deaths

Severe disease and death in immunocompromised individuals

# Varicella vaccine

- Live attenuated strain derived from the Oka strain of VZV
- Contraindicated in pregnancy and in individuals with primary or acquired immunodeficiency, or individuals on immunosuppressive therapy
- No adverse outcomes identified so far with inadvertent vaccination in pregnancy
- Widely used in children in the USA and Japan for many years

# Protection from disease

- 2-dose vaccination schedule in adults provides 70% protection against typical Varicella disease
- Single dose schedule in children provides 90% protection
- Break-through infections are modified – individuals who contract wild-type varicella have fewer lesions and less systemic upset
- Oka strain can establish latency, and result in herpes zoster
- Oka strain is sensitive to aciclovir

# Current UK recommendations for the use of Varicella vaccine

- 2 doses for adults, 1 dose for <13 years
- Groups to be vaccinated
  - Seronegative healthcare workers
  - Susceptible family contacts of high-risk immunocompromised patients

# Health Care Workers - why vaccinate?

- Non-immune HCWs can pose a significant health risk to high risk patients e.g. immunocompromised, pregnant or neonates

- Non-immune healthcare workers who are susceptible are at risk of being infected by their patients

# Possible adverse effects of mass VZV vaccination

- Is there a risk that vaccination of infants will lead to an increase in severe disease in adults?

- Exposure to Varicella boosts immunity to herpes zoster (Brisson et al Vaccine 2002,Thomas et al Lancet 2002)

  ⇓

- Mass varicella vaccination may cause a major epidemic of herpes-zoster.

# USA update on varicella vaccine

- A decade of varicella prevention in the United States has resulted in a dramatic decline in disease
- However, even with high vaccination coverage, the effectiveness of 1 dose of vaccine did not generate sufficient population immunity to prevent community transmission.
- 2-dose varicella vaccine schedule, therefore recommended for children in 2006.
- Data remain inconclusive regarding an effect of the varicella vaccination program on herpes zoster epidemiology.

# USA continued…

VZV vaccine in the elderly (>60) markedly reduces morbidity from herpes zoster, and post-herpetic neuralgia (P<0.001) (Oxman et al, NEJM 2005)

In October 2006 the Advisory Committee on Immunization Practices (ACIP) recommended HZ vaccination of persons aged >/=60 years; these recommendations were published in 2008.

# European working group on Varicella consensus statement (2004)

Routine VZV immunisation recommended for:

- infants between 12 and 18 months
- all susceptible children before their 13th birthday
- catch-up vaccination in older children and adults who have no reliable history of varicella and who are at high risk of transmission and exposure.

Universal immunisation of children is not currently a UK recommendation

# INFLUENZA VIRUS

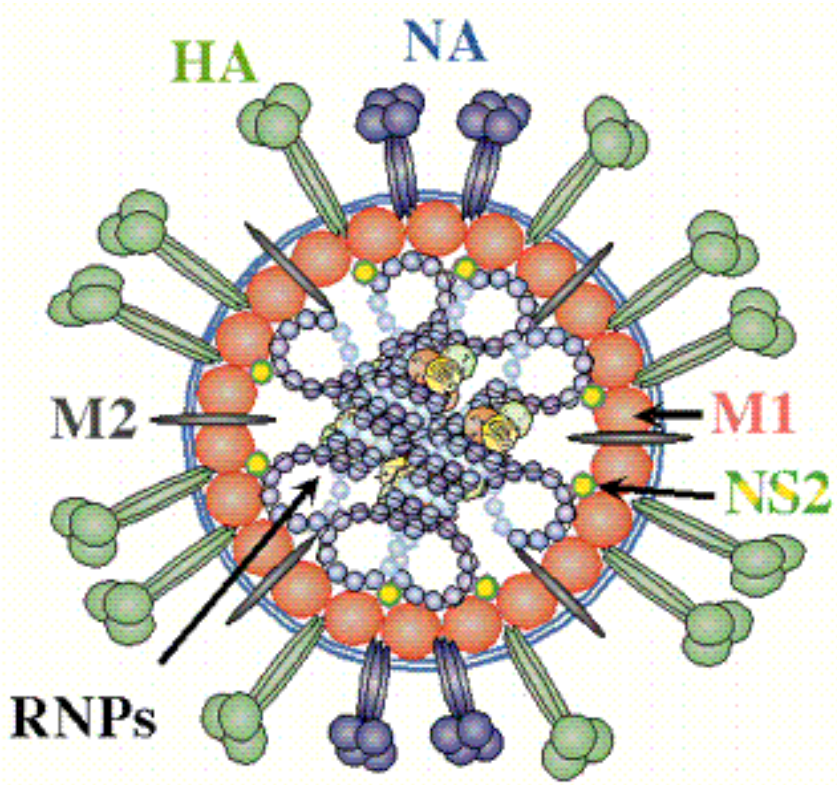
**Orthomyxovirus**

Genome consists of 8 fragments of negative sense ss-RNA

Viral envelope contains 2 glycoproteins

Haemagglutinin (H)
Neuraminidase (N)

and is lined by the matrix (M1) and membrane (M2) proteins



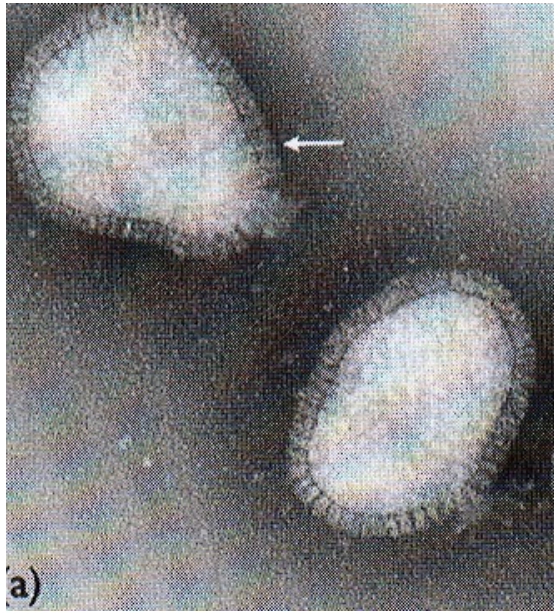
# Classification of influenza

Three types:

Type A infects man and animals
e.g. pigs, horses, ducks and birds

Type B infects man only

Type C doubtful pathogenicity



# Antigenic changes in influenza

Envelope proteins vary their structure by two different mechanisms :

Antigenic SHIFT and Antigenic DRIFT

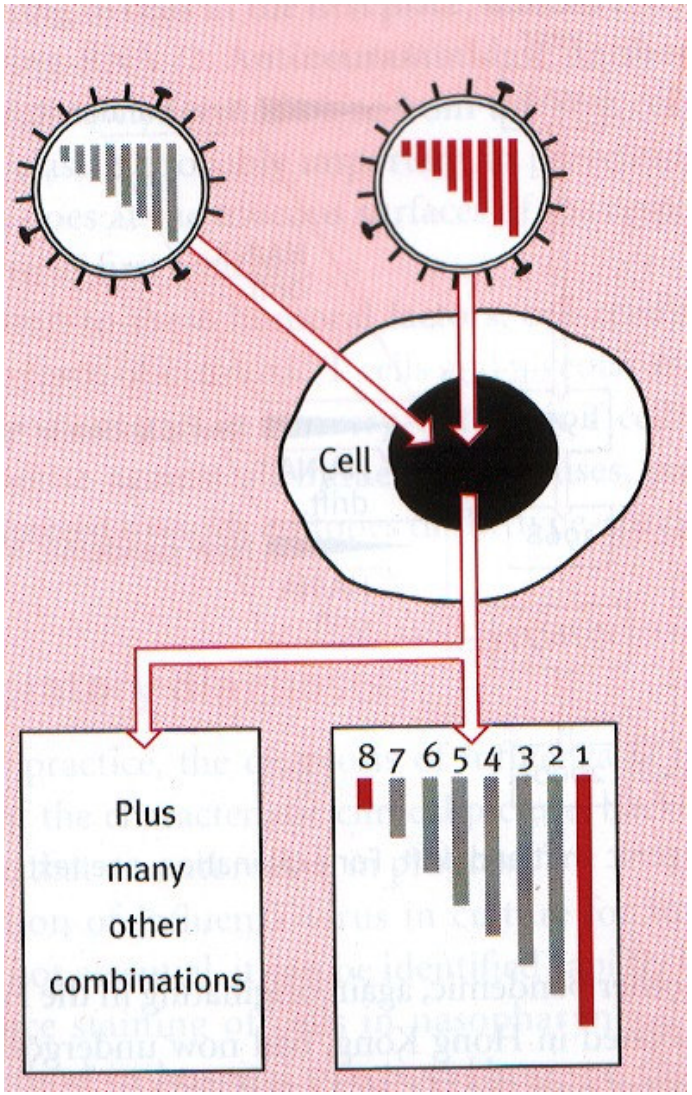
allowing the virus to escape neutralisation by the immune system

# Antigenic shift

This is caused by dual infection with influenza A, almost certainly in pigs; e.g. simultaneous infection with a bird and human strain.

Both viruses may RANDOMLY EXCHANGE segments of RNA.

When such radically different viruses appear for the first time they have epidemic and pandemic potential

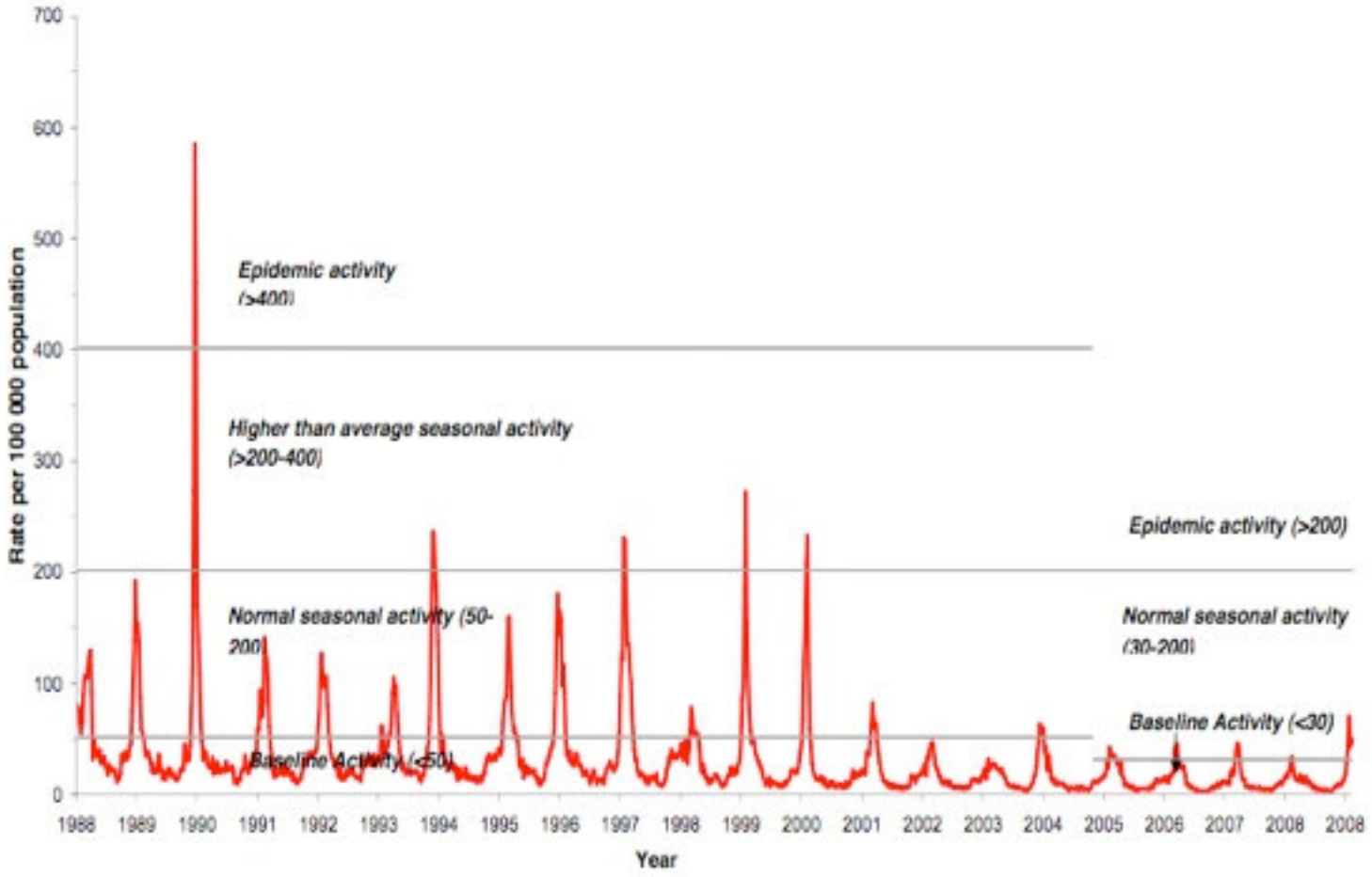


# Antigenic drift

- influenza RNA polymerase makes copying errors.
- leads to changes in the nucleotide sequence of genes encoding envelope proteins.
- selective "pressure" from antibody leads to the selection of strains which are not neutralised because of changes in the antigenic structure of these proteins.

# Seasonal influenza


# RCGP weekly consultation rate for influenza-like illness, England




*Thresholds were revised for the 2004/05 season onwards. There has been a secular decline in GP consultation rates for ILI over recent years. *See CDPH 2003; 6(3): 238-45.*

# Prevention of influenza - Influenza Vaccine

- Current vaccines are trivalent (2 type A viruses and 1 type B)

- Viruses are grown in embryonated hens' eggs, chemically inactivated and further purified

# Flu Vaccine Composition for 2008/09 season

A WHO committee review annually the composition of vaccines for the next year.

WHO has recommended that the 2008/09 trivalent influenza vaccine for the northern hemisphere winter contains:

- A/Brisbane/59/2007 (H1N1)-like virus
- A/Brisbane/10/2007 (H3N2)-like virus

- B/Florida/4/2006-like virus

# Efficacy

- Current vaccines give 70-80% protection against well matched strains of wild-type influenza
- 2007/08 - strains not well matched - 40% protection
- Protection lasts for about one year
- In the elderly, immunisation reduces the incidence of bronchopneumonia, hospital admissions and mortality
- Vaccination of health care workers
  - reduces influenza infection in long stay elderly care wards
  - prevents influenza infection in health care workers
  - may reduce reported days of work absence and febrile respiratory illness.

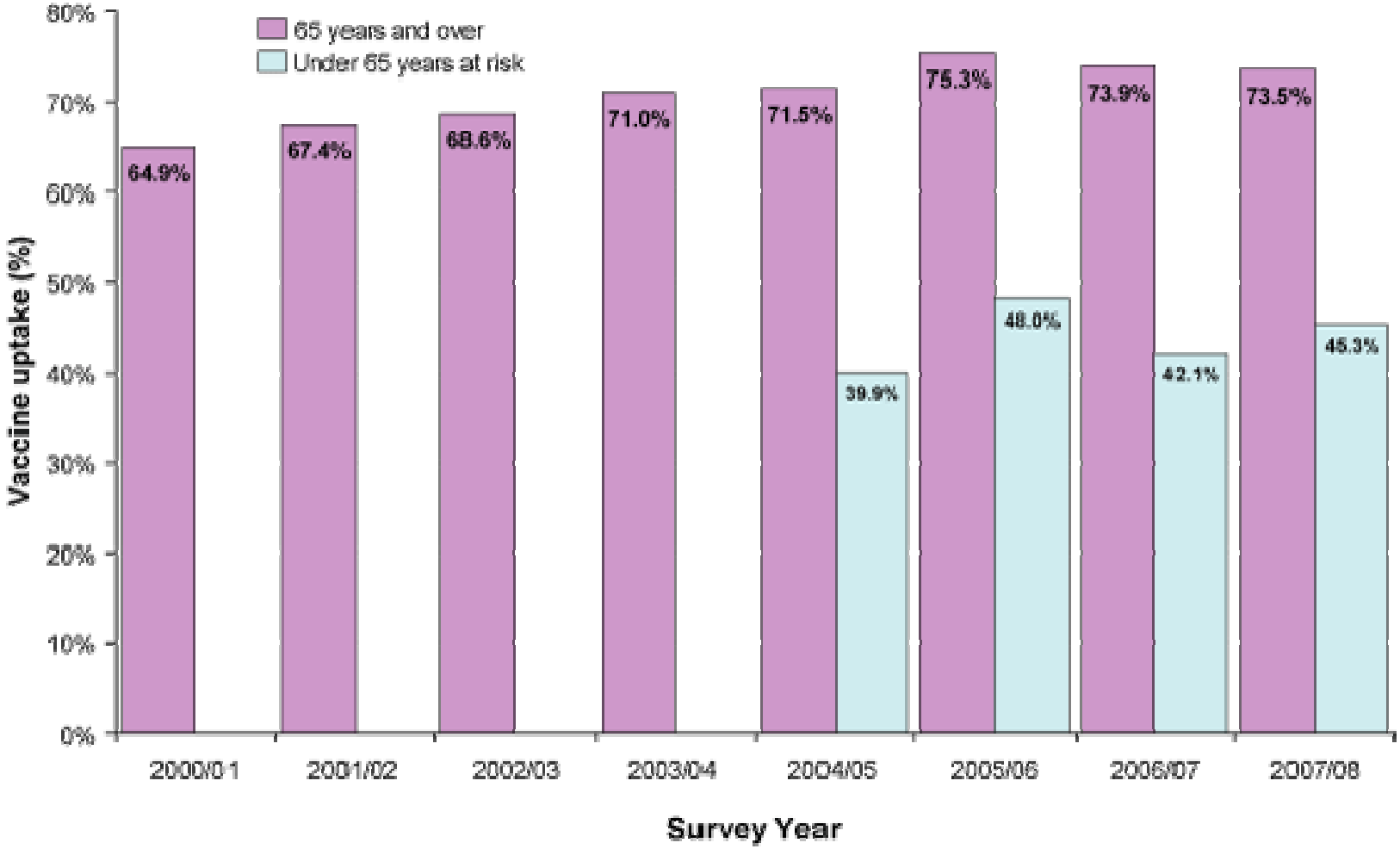
# Influenza vaccine programme in care home staff

- Hayward et al BMJ 2006;333:1241-4
- Aim: to determine whether influenza vaccination of care home staff indirectly protects residents
- Intervention and control care homes, 1703 staff and 2604 residents, 2 seasons 2003-4, 2004-5
- Number of staff vaccinations required to prevent (during the influenza season):
  - One death 8
  - One influenza-like illness 5 (p=0.004)
  - GP consultation for ILI 6 (p=0.008)
  - Hospital admission with ILI 20 (p=0.009)

# Current UK recommendations for influenza vaccine

- All aged >65 years
- All aged > 6 months (including pregnant women) with:
  - Chronic heart, renal, liver or respiratory disease
  - Diabetes
  - Immunosuppression due to disease or treatment (including HIV)
- Health care workers
- Those in long stay residential homes
- Carers of elderly or disabled persons

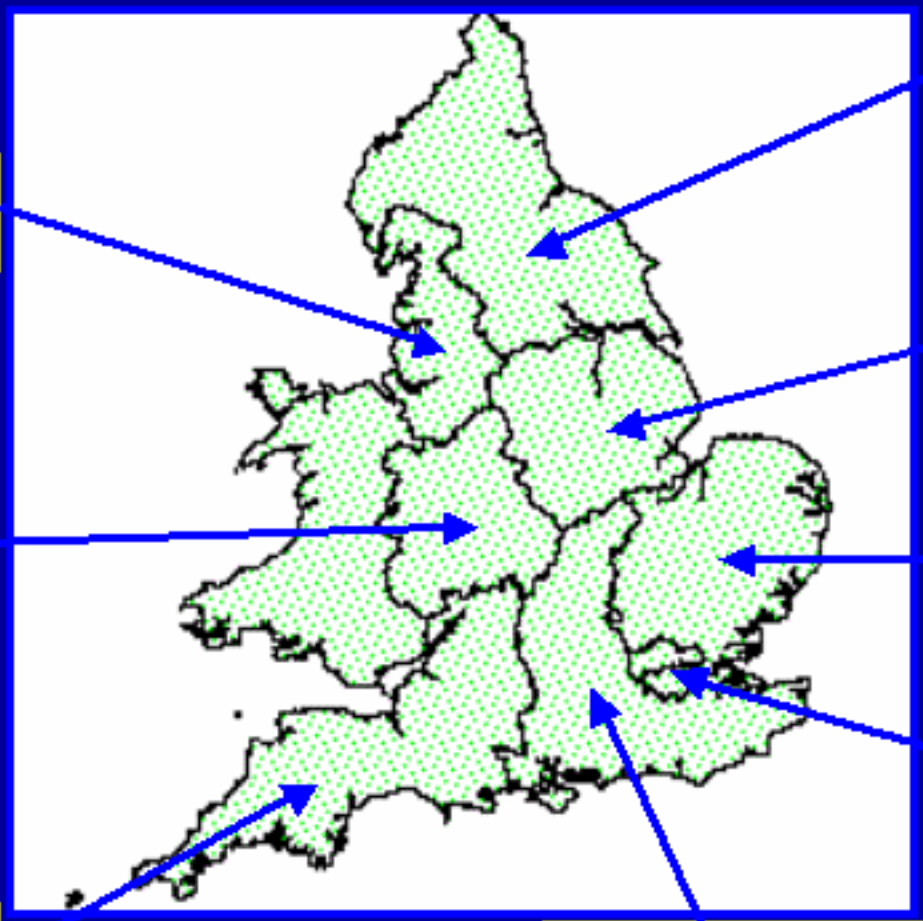
# Vaccine uptake in the UK



# Uptake in those aged six months to under 65 in a risk group for 2005/06 survey

| | Uptake % |
|---|---|
| Chronic Respiratory Disease | 42% |
| Chronic Heart Disease | 51% |
| Chronic Renal Disease | 36% |
| Diabetes | 69% |
| Immunosuppression | 39% |
| Chronic Liver Disease | 26% |

# Vaccine Uptake in Health Care Workers 2001/02 (18% overall)



Northern & Yorkshire *11%*

North West *26%*

Trent *13%*

West Midlands *33%*

Eastern *20%*

London *10%*

South & West *15%*

South East *21%*

# Prevention of influenza - antivirals

Drugs currently recommended for prophylaxis are **Oseltamivir and Zanamivir (NICE 2008)**

**Current recommendation in seasonal influenza:**

Used in at-risk individuals when influenza A or B is circulating in the community above baseline levels:

**and**

Have not had an influenza vaccination, or had it within last two weeks or Influenza vaccine given did not match circulating virus

**and**

In close contact with influenza-like symptoms

**and**

Can start drug within 48 hours

# Anti-viral drugs available for Influenza Treatment

Treatment must be commenced within 1-2 days if any benefit is to be seen.

**Amantadine** or **Rimantadine**

- inhibit viral replication (block ion channel formed by M2 protein)
- Active against Influenza A only
- resistance to both these drugs occurs early in treatment and such strains are transmissible and pathogenic.

**Zanamivir** (Relenza) and **Oseltamivir** (Tamiflu).

- neuraminidase inhibitors, preventing virus penetration and blocking the release of viral particles.
- reduce symptoms by one day.

# Current circulating viruses

- Current circulating strains in the UK 2008/09 are H1 and H3 and are well matched to vaccine strains

- H3
  - 101 influenza A (H3) specimens have been tested for anti-viral drug resistance since week 40/08
    - 100% resistant to amantadine
    - of these 74 have been tested and found sensitive to oseltamivir and zanamivir.
- H1
  - Forty influenza A (H1) specimens have been tested for anti-viral drug resistance since week 40/08
    - 39 (97.5%) of these were resistant to oseltamivir
    - all were sensitive to zanamivir and amantadine.

# Hepatitis ?cause

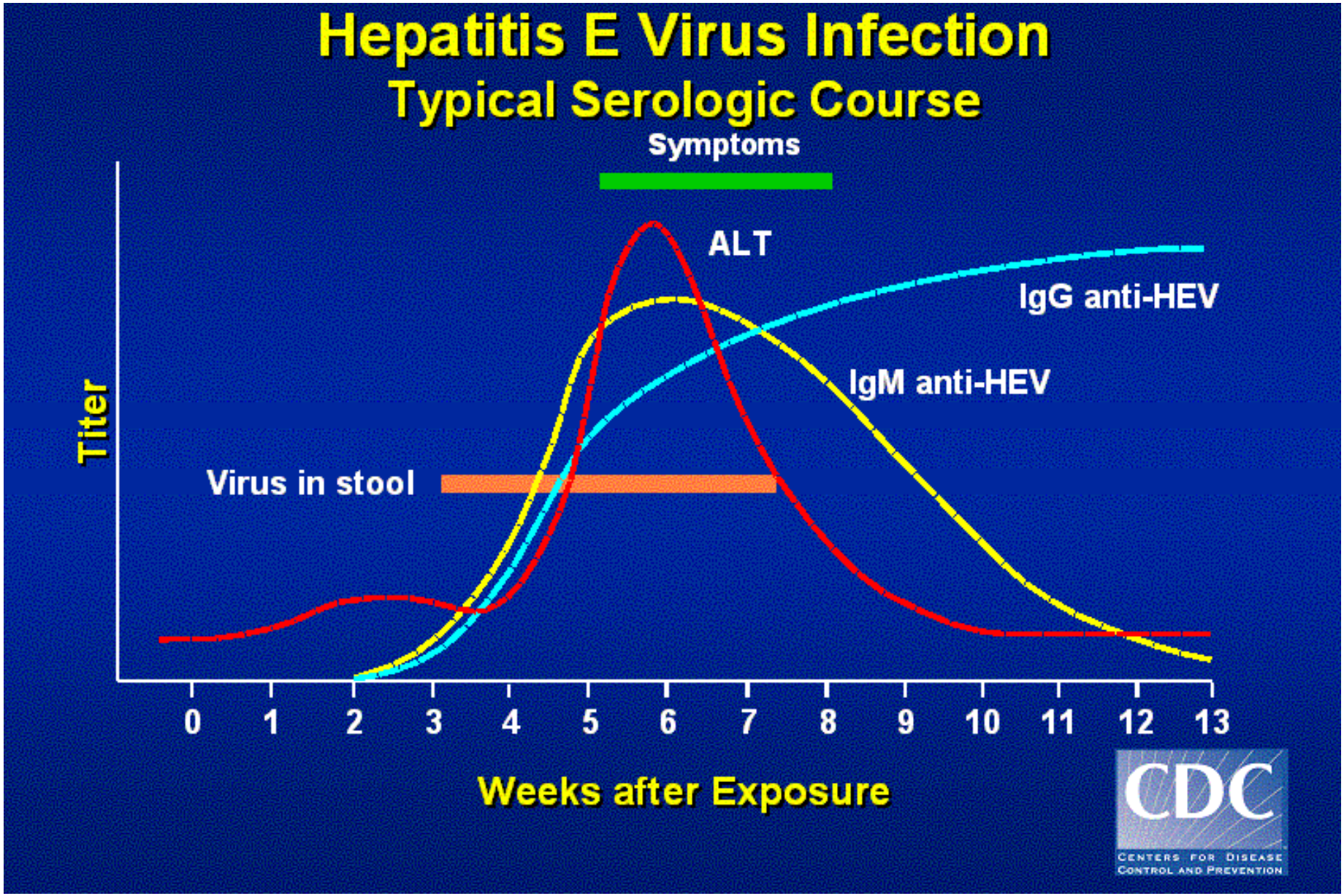
- 74 year old man
- 7 day history of increasing malaise
- 2 days of dark urine
- Wife says he looks yellow
- No significant past medical history
- O/E jaundiced, generally unwell, tender RUQ
- LFTS – Bili 104, ALT 2346, AlkP 346, Alb 42

# Hepatitis E

- Clinical features
  - Very similar to Hepatitis A
  - Incubation period longer (about 6 weeks)
  - High mortality in pregnancy (20%)
  - Fulminant hepatitis more common

# Hepatitis E - epidemiology

- Outbreaks in most developing countries especially Bangladesh, India
- Recent cases diagnosed in the UK
- Diagnose by detection of anti-hepatitis E antibody
- No vaccine or specific treatment available
- Control in developing countries depends on maintaining clean water supply


Hepatitis E Virus Infection
Typical Serologic Course
Symptoms
ALT
IgG anti-HEV
IgM anti-HEV
Virus in stool
Titer
0 1 2 3 4 5 6 7 8 9 10 11 12 13
Weeks after Exposure
CDC
Centers for Disease Control and Prevention

# Current hepatitis B case

- 48 year old bus driver
- HBsAg performed after LFTs were checked as he was non-specifically unwell (ALT 1500)
  - HBsAg positive
  - HBeAg positive
  - ante-HBcore IgG positive

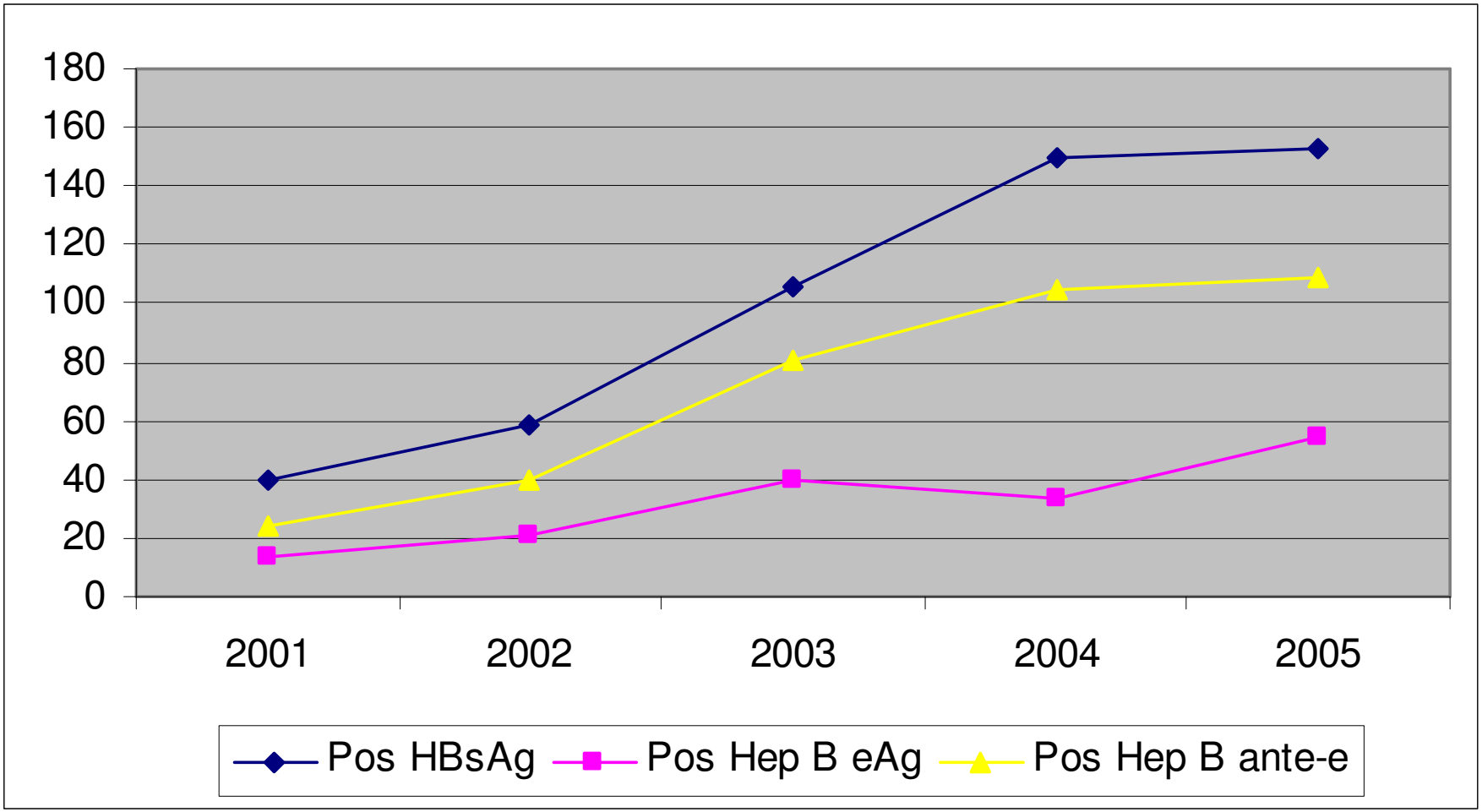
# Oxford Times Jan 30th 2009

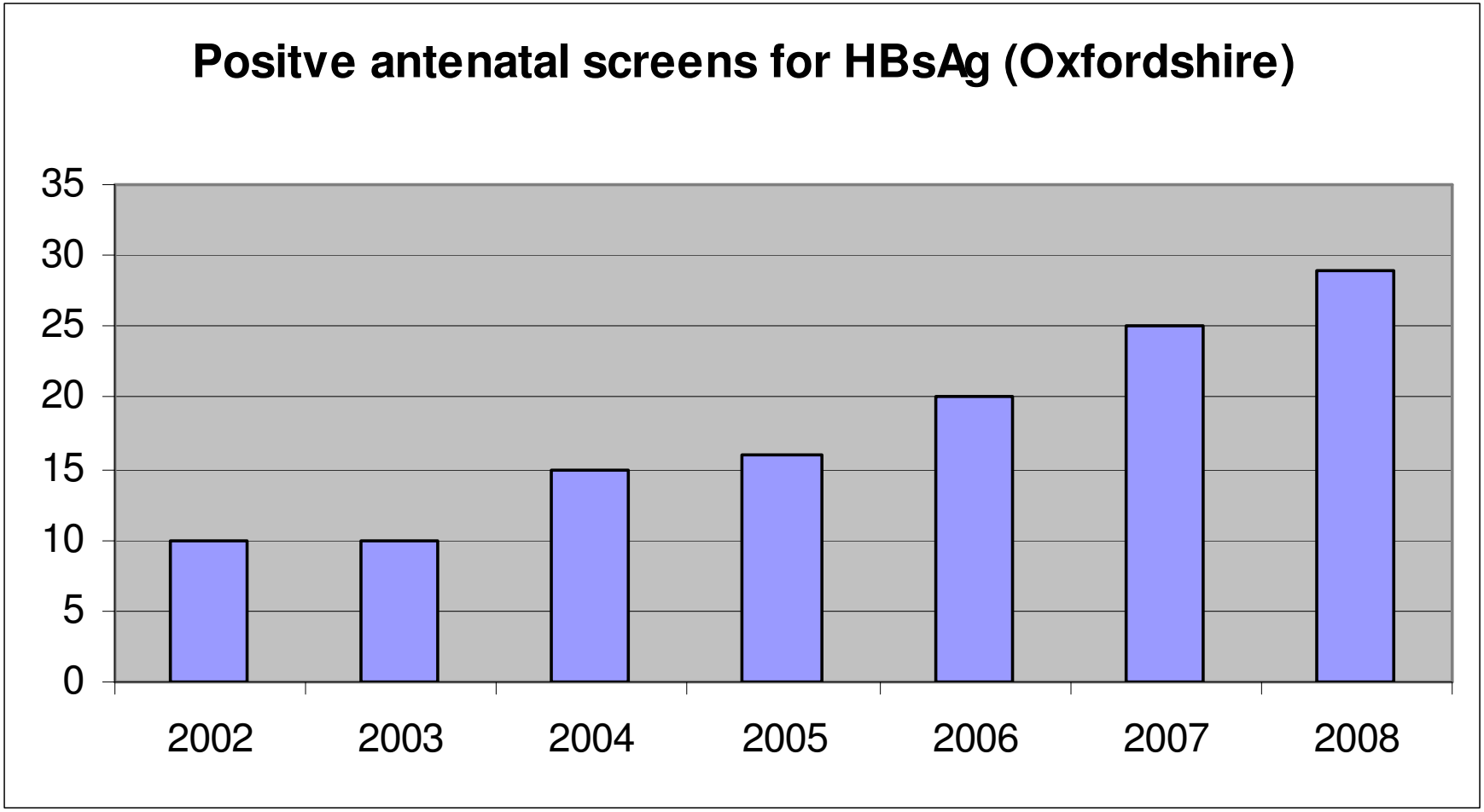
## Confirmed hepatitis cases are on rise across region

*OXFORDSHIRE:* The number of cases of hepatitis B reported in the Thames Valley area rose by 360 per cent in one year. Cases of the viral infection, which can cause long-term liver damage, rose from 30 in 2006 to 138 in 2007, the latest year for which figures are available.Ten years earlier, in 1997, the number of recorded cases was just 18.

South Central Strategic Health Authority, which covers Oxfordshire, said the rise in cases reported to the Health Protection Agency was due to improved testing in higher-risk populations, so that cases which might previously have gone unrecorded were now being counted.

# Hepatitis B – new laboratory diagnoses (Oxfordshire)




Positve antenatal screens for HBsAg (Oxfordshire)
35
30
25
20
15
10
5
0
2002
2003
2004
2005
2006
2007
2008